Matrix metalloproteinase degradation of extracellular matrix in tumor growth

Beamline: U10B

Technique: Infrared microspectroscopy

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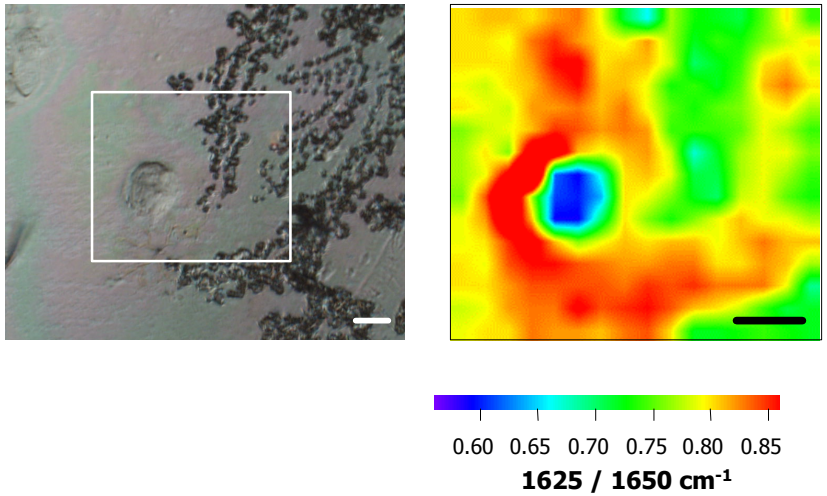
Motivation: Matrix Metalloproteinases (MMPs) are cell-secreted soluble and membrane-tethered enzymes that degrade extracellular matrix (ECM) proteins. These proteases play a key role in diverse physiological and pathological processes, including embryonic development, wound repair, inflammatory diseases and cancer. Yet, there is insufficient knowledge on the mode by which cell-produced MMPs conduct their action on the ECM. Specifically, questions on (1) what are the induced structural and chemical changes on the collagen-based macromolecules of the ECM and (2) the localization of the degradation activity within the pericellular space, are of great interest.



(Left) (A) Optical image of live HT1080 cells on a matrigel matrix. The white box indicates the area imaged with the IR microscope. (Right) IR image of the same cell and its surroundings as calculated from the "triple helix unwinding" ratio of 1625 / 1650 cm^{-1}. The blue area surrounded by a green boundary represents the detected HT1080 cell. The red areas around the cell represent the degraded matrigel matrix. Scale bar is 20 microns.

Results: To provide new insights to these questions, we utilized Fourier transform infrared (FTIR) micro-spectroscopy imaging to study proteolytic processes, induced by invasive cancer cells, on collagen-based matrices. The application of FTIR spectroscopy to the study of MMPs proteolysis is advantageous since it provides chemical and structural information as opposed to the other used methods. We show that the degradation of the biological matrix proteins by MMPs is executed by limited proteolysis in contrast to extensive degradation of the polypeptide chains. This limited proteolysis results in unwinding of local triple-helices within the collagen network, which leads to the destabilization of the biological matrix. Furthermore, the degradation patterns localized by FTIR imaging show different levels of MMPs activity within the pericellular space.